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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,088	01/14/2002	Robert C. Getts	4081.010	6251

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EXAMINER	
CHAKRABARTI, ARUN K	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/050,088	Getts
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 22, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11 and 13-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11 and 13-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Current status of the Application

1. Applicant's amendment received on September 23, 2003 has been entered. Claims 1 and 2 have been amended. Claim 12 has been canceled without prejudice towards further prosecution. Claims 1-11 and 13-24 are currently pending in this application.

Specification

2. Claim 1 has been objected to because the word "said" has been repeated twice in section (b) of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-3, 6-11, 16, 18, 19, 23, and 24 are rejected under 35 U.S.C. 103(a) as being obvious over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001) in view of Weisburg et al. (U.S. Patent 6,280,952 B1) (August 28, 2001).

Hellyer et al teach a method for determining the presence of at least one specific nucleotide sequence in a target nucleic acid reagent extracted from a biological sample (abstract), the method comprising the steps of:

a) contacting a microarray with:

(I) a target nucleic acid reagent, the target nucleic acid reagent having a nucleotide sequence, the nucleotide sequence further including a capture sequence (Column 16, lines 1-40, and Example 5);

(ii) a capture reagent, the capture reagent having at least one first arm having a label capable of emitting a detectable signal and at least one second arm having a nucleotide sequence complementary to the capture sequence of the target nucleic acid reagent (Example 5);
the microarray having thereon a plurality of features, each of the plurality of features including a probe nucleotide sequence; and

b) treating the microarray from step a) at a temperature and for a time sufficient to induce the nucleotide sequence of the target nucleic acid to hybridize to the probe nucleotide sequence complementary thereto on the microarray, and to induce the capture reagent to hybridize to the

capture sequence of the nucleotide sequence of the target nucleic acid hybridized to the microarray (Example 5, and Column 13, line 63 to column 14, line 9).

Hellyer et al teach a method, wherein the presence of the latter hybridization results in the emission of the detectable signal from the corresponding feature, and in the absence thereof results in no emission of the detectable signal from the corresponding feature, thus generating a detectable hybridization pattern for subsequent analysis (Column 16, lines 24-40, and Example 5).

Hellyer et al teach a method, wherein the microarray is incubated at a first temperature for a first period of time and thereafter at a lower second temperature for a second period of time which may be different than the first period of time that are suitable for hybridization of the target nucleic acid reagent to the capture reagent (Example 5).

Hellyer et al teach a method, further comprising the step of utilizing a spin column to prepare the target nucleic acid reagent prior to step (a) ((Example 5, column 20, lines 28-30).

Hellyer et al do not teach the method of carrying out the hybridization condition at multiple temperatures, wherein the treatment comprises application of one temperature for a time sufficient to induce the target nucleic acid to hybridize to the probe nucleotide sequence and comprises application of a second temperature for a time sufficient to induce the capture reagent to hybridize to the capture sequence, the hybridization being induced in any order and wherein first temperature ranges from 65 degree centigrade to 75 degree centigrade or about 32 degree centigrade and the second temperature ranges from 50 degree centigrade to 55 degree centigrade and the first period of time is overnight and the second period of time is 4 to 6 hours.

Weisburg et al. teach the method of carrying out the hybridization condition at multiple temperatures, wherein the treatment comprises application of one temperature for a time sufficient to induce the target nucleic acid to hybridize to the probe nucleotide sequence and comprises application of a second temperature for a time sufficient to induce the capture reagent to hybridize to the capture sequence, the hybridization being induced in any order and wherein first temperature ranges from 65 degree centigrade to 75 degree centigrade or about 32 degree centigrade and the second temperature ranges from 50 degree centigrade to 55 degree centigrade and the first period of time is overnight and the second period of time is 4 to 6 hours. (Abstract and Examples 3 and 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method of carrying out the hybridization condition at multiple temperatures, wherein the treatment comprises application of one temperature for a time sufficient to induce the target nucleic acid to hybridize to the probe nucleotide sequence and comprises application of a second temperature for a time sufficient to induce the capture reagent to hybridize to the capture sequence of Weisburg et al in the method of Hellyer et al , since Weisburg et al. state, "These methods are particularly useful as part of a diagnostic assay in which the target polynucleotide is amplified to produce larger amounts of amplified nucleic acids which are free in solution (Column 9, lines 58-61)." An ordinary practitioner would have been motivated to combine and substitute the method of carrying out the hybridization condition at multiple temperatures, wherein the treatment comprises application of

one temperature for a time sufficient to induce the target nucleic acid to hybridize to the probe nucleotide sequence and comprises application of a second temperature for a time sufficient to induce the capture reagent to hybridize to the capture sequence of Weisburg et al in the method of Hellyer et al , in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Weisburg et al., of an invention which is particularly useful as part of a diagnostic assay in which the target polynucleotide is amplified to produce larger amounts of amplified nucleic acids which are free in solution.

Although Weisburg et al and Hellyer et al may not have taught of concurrently contacting the microarray containing the probes with the target and the capture probe, this rejection is based on the fact that the order of adding ingredients is *prima facie* obvious as MPEP 2144.04 states, " *In re Gibson,* 39 F.2d 975, 5 USPQ 230 (CCPA 1930) Selection of any order of mixing ingredients is *prima facie* obvious".

5. Claim 5 is rejected under 35 U.S.C. 103(a) over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001) in view of Weisburg et al. (U.S. Patent 6,280,952 B1) (August 28, 2001) further in view of Kayyem et al. (U.S. Patent 6,290,839 B1)(September 18, 2001).

Hellyer et al in view of Weisburg et al. teach the method of claims 1-3, 6-11, 16, 18, 19, 23, and 24 as described above.

Hellyer et al in view of Weisburg et al. do not teach the method wherein the capture reagent is a dendrimer.

Kayyem et al teach the method wherein the capture reagent is a dendrimer (Column 52, lines 27-43, and column 59, lines 18-42).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the capture reagent is a dendrimer of Kayyem et al in the method of Hellyer et al in view of Weisburg et al., since Kayyem et al. state, "Adding extra linking sequences between the probe nucleic acid and the ETMs can result in the ETMs being spatially closer to the surface, giving better results (Column 59, lines 31-34)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the capture reagent is a dendrimer of Kayyem et al in the method of Hellyer et al in view of Weisburg et al. in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Kayyem et al., of an invention which provides addition of extra linking sequences between the probe nucleic acid and the ETMs that can result in the ETMs being spatially closer to the surface, giving better results.

6. Claims 4, 13-15, 17, and 20-22 are rejected under 35 U.S.C. 103(a) over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001) in view of Weisburg et al. (U.S. Patent 6,280,952 B1) (August 28, 2001) further in view of Lipshutz et al. (U.S. Patent 6,280,950 B1) (August 28, 2001).

Hellyer et al in view of Weisburg et al. teach the method of claims 1-3, 6-11, 16, 18, 19, 23, and 24 as described above.

Hellyer et al in view of Weisburg et al. do not teach the method wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence.

Lipshutz et al teach the method wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence (Column 8, lines 13-36).

Hellyer et al in view of Weisburg et al. do not teach the method wherein the first temperature of hybridization is below the melt temperature of the blocking oligonucleotide and the second temperature of hybridization is above the melt temperature of the blocking oligonucleotide.

Lipshutz et al teach the method wherein the temperature of hybridization can be optimized depending on the length and sequence of the target nucleic acid (Column 7, lines 9-33).

Hellyer et al in view of Weisburg et al. do not teach the method wherein the target nucleic acid is cDNA.

Lipshutz et al teach the method wherein the target nucleic acid is cDNA (Column 9, line 62 to column 10, line 13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence and the optimization of hybridization temperature depending on the length and sequence of the target nucleic acid of Lipshutz et al. in the method of Hellyer et al.in view of Weisburg et al.,

since Lipshutz et al. state, "For example, when it is desired to detect a particular (target) nucleic acid that is expressed at low levels in a nucleic acid sample, selective elimination of other nucleic acids that are present in high level in the sample can improve detection and isolation of the target sequence. In this case, a nucleic acid pool containing nucleic acids complementary to the nucleic acids it is desired to block in the sample can be hybridized to the sample. The nucleic acid pool (blocking reagent) will hybridize to complementary sequences in the sample, form stable hybrid duplexes, and thereby prevent interaction (e.g., nonspecific binding) of the blocked nucleic acids with the capture sequence (Column 8, lines 17-29)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence and the optimization of hybridization temperature depending on the length and sequence of the target nucleic acid of Lipshutz et al. in the method of Hellyer et al. in view of Weisburg et al., in order to improve the process for detection of a target nucleic acid and also in order to achieve the express advantages, as noted by Lipshutz et al., of an invention which provides prevention of interaction (e.g., nonspecific binding) of the blocked nucleic acids with the capture sequence and selective elimination of other nucleic acids that are present in high level in the sample thereby improving detection and isolation of the target sequence.

Response to Amendment

7. In response to amendment, previous 102 and 103 rejections are hereby withdrawn. However, new 103(a) rejections are hereby included.

Response to Arguments

8. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

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